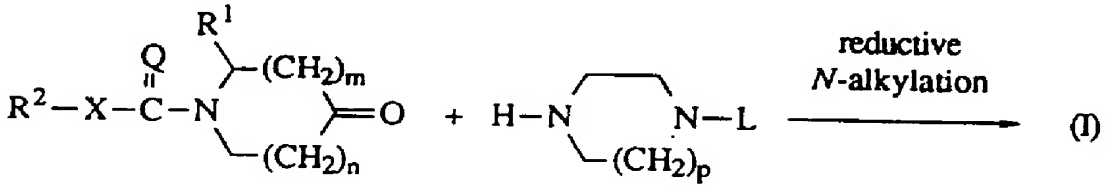
Amendments to the Specification:

At page 28, please amend lines 11-14 as follows:

The preparation of intermediate compounds (XI) and (XII) and other intermediates is described in WO 97/16440-A1, published May 9, 1997 by Janssen Pharmaceutica N.V., which is incorporated ~~disclosed~~ herein by reference as well as in ~~other publications mentioned in WO 97/16440-A1, such as, e.g.~~ EP-0,532,456-A and U.S. Pat. No. 5,310,743. The relevant sections of WO 97/16440-A1 are reproduced below:

After the paragraph at page 28, lines 11-14, please insert the following:

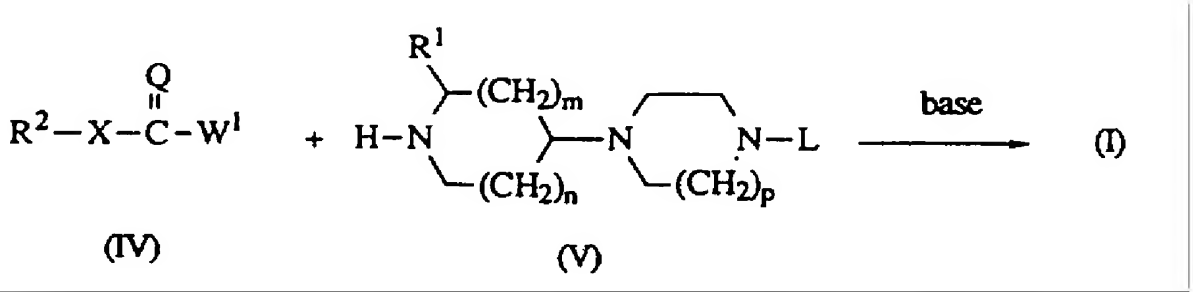
The compounds of formula (I) can be prepared by reductively *N*-alkylating an intermediate of formula (III) with an intermediate of formula (II). Said reductive *N*-alkylation may be performed in a reaction-inert solvent such as, for example, dichloromethane, ethanol, toluene or a mixture thereof, and in the presence of an appropriate reducing agent such as, for example, a borohydride, e.g. sodium borohydride, sodium cyanoborohydride or triacetoxy borohydride. In case a borohydride is used as a reducing agent, it may be convenient to use a complex-forming agent such as, for example, titanium(IV)isopropylate as described in J. Org. Chem, 1990, *55*, 2552-2554. Using said complex-forming agent may also result in an improved *cis/trans* ratio in favour of the *trans* isomer. It may also be convenient to use hydrogen as a reducing agent in combination with a suitable catalyst such as, for example, palladium-on-charcoal or platinum-on-charcoal. In case hydrogen is used as reducing agent, it may be advantageous to add a dehydrating agent to the reaction mixture such as, for example, aluminium *tert*-butoxide. In order to prevent the undesired further hydrogenation of certain functional groups in the reactants and the reaction products, it may also be advantageous to add an appropriate catalyst-poison to the reaction mixture, e.g., thiophene or quinoline-sulphur. Stirring and optionally elevated temperatures and/or pressure may enhance the rate of the reaction.



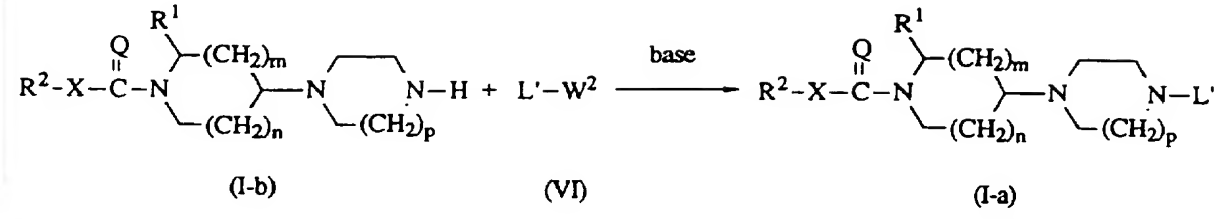
(II) (III) (I)

In this and the following preparations, the reaction products may be isolated from the reaction medium and, if necessary, further purified according to methodologies generally known in the art such as, for example, extraction, crystallization, trituration and chromatography.

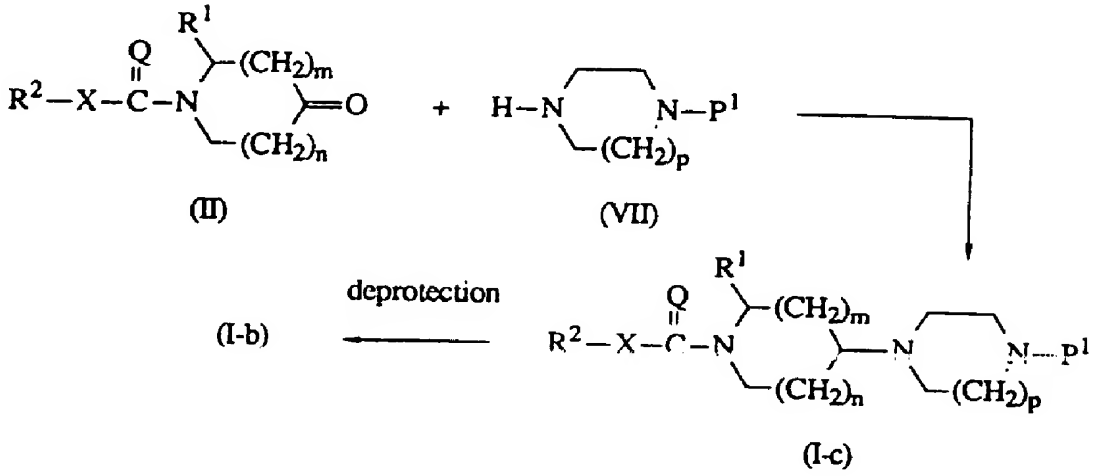
The compounds of formula (I) can also be prepared by reacting an intermediate of formula (IV) wherein W^1 is an appropriate leaving group such as, for example, a halogen, e.g. chloro or bromo, or a sulfonyloxy leaving group, e.g. methanesulfonyloxy or benzenesulfonyloxy, with an intermediate of formula (V). The reaction can be performed in a reaction-inert solvent such as, for example, a chlorinated hydrocarbon, e.g. dichloromethane, an alcohol, e.g. ethanol, or a ketone, e.g. methyl isobutylketone, and in the presence of a suitable base such as, for example, sodium carbonate, sodium hydrogen carbonate or triethylamine. Stirring may enhance the rate of the reaction. The reaction may conveniently be carried at a temperature ranging between room temperature and reflux temperature.



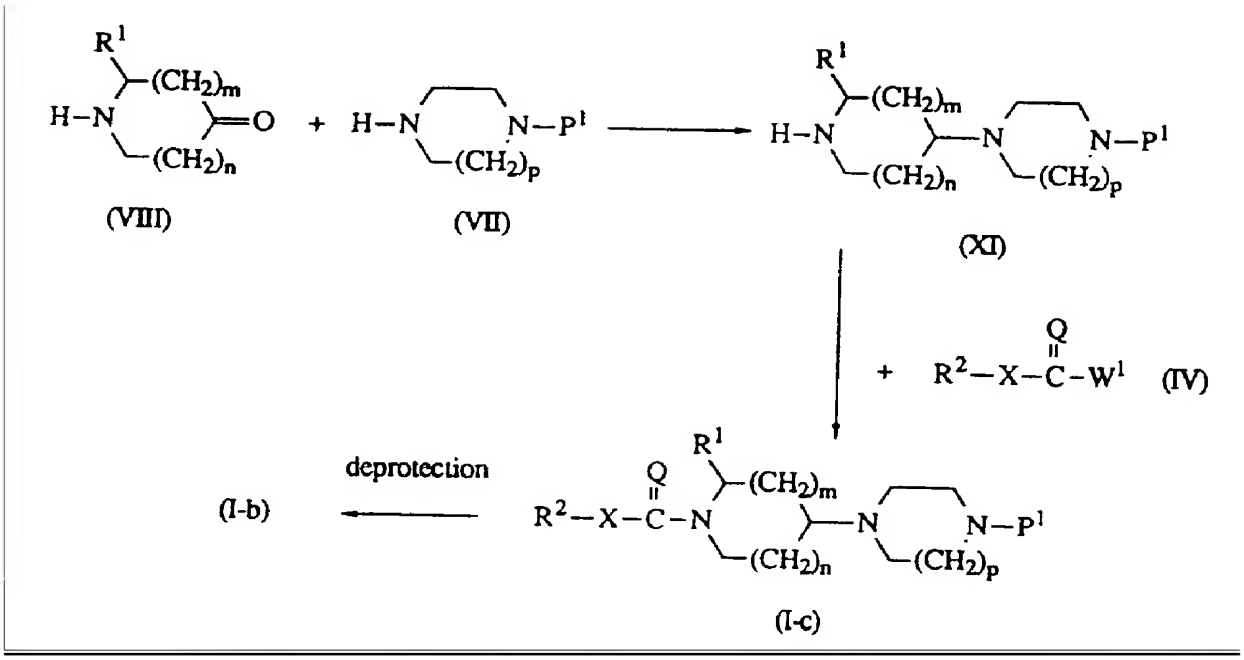
The compounds of formula (I) may also be converted into each other following art-known transformations. In particular, the compounds of formula (I) wherein L is other than hydrogen, said L being represented by L' and said compounds being represented by formula (I-a), can also be prepared by reacting a compound of formula (I) wherein L is hydrogen, said compounds being represented by formula (I-b), with an intermediate of formula (VI) wherein W^2 is an appropriate leaving group such as, for example, a halogen, e.g. chloro or bromo, or a sulfonyloxy leaving group, e.g. methanesulfonyloxy or benzenesulfonyloxy, at reaction conditions which are similar to those for the reaction between intermediates of formula (IV) and (V).



Compounds of formula (I-b) may be prepared by reductively *N*-alkylating a piperazine derivative of formula (VII) wherein P^1 is a protective group such as, for example, benzyl, with an intermediate of formula (II). Said reaction may be performed in a similar way as described hereinabove for the reductive *N*-alkylation using intermediates (II) and (III). The thus formed compound of formula (I-c) may then be deprotected using art-known deprotection techniques. Depending on the nature of the protective group P^1, compounds of formula (I-c) may be part of the scope of the compounds of formula (I).



Alternatively, compounds of formula (I-b) may be prepared by first reductively *N*-alkylating a piperazine derivative of formula (VII) wherein P^1 is a protective group such as, for example, halo, with an intermediate of formula (VIII) using the same procedure as described hereinabove for the reductive *N*-alkylation using intermediates (II) and (III). The thus formed intermediate of formula (XI) may then be reacted with an intermediate of formula (IV) in a reaction-inert solvent and optionally in the presence of a suitable base such as, for example, triethylamine, to form a compound of formula (I-c), which may then be deprotected using art-known deprotection techniques.

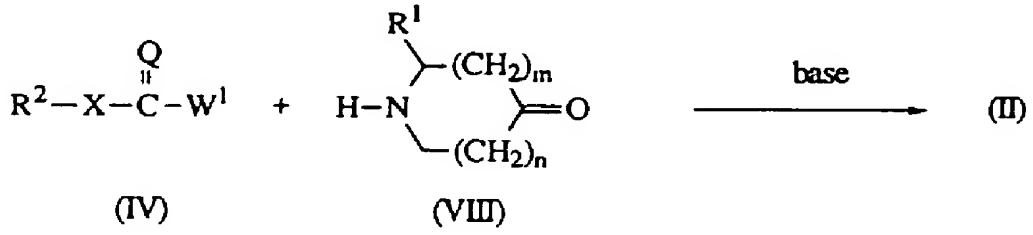


The compounds of formula (I-b) are deemed to be of particular use in the synthesis of other compounds of formula (I).

The compounds of formula (I) may also be converted to the corresponding *N*-oxide forms following art-known procedures for converting a trivalent nitrogen into its *N*-oxide form. Said *N*-oxidation reaction may generally be carried out by reacting the starting material of formula (I) with an appropriate organic or inorganic peroxide. Appropriate inorganic peroxides comprise, for example, hydrogen peroxide, alkali metal or earth alkaline metal peroxides, e.g. sodium peroxide, potassium peroxide; appropriate organic peroxides may comprise peroxy acids such as, for example, benzenecarboperoxoic acid or halo substituted benzenecarboperoxoic acid, e.g. 3-chlorobenzenecarboperoxoic acid, peroxoalkanoic acids, e.g. peroxoacetic acid, alkylhydroperoxides, e.g. *tert*-butyl hydroperoxide. Suitable solvents are, for example, water, lower alkanols, e.g. ethanol and the like, hydrocarbons, e.g. toluene, ketones, e.g. 2-butanone, halogenated hydrocarbons, e.g. dichloromethane, and mixtures of such solvents.

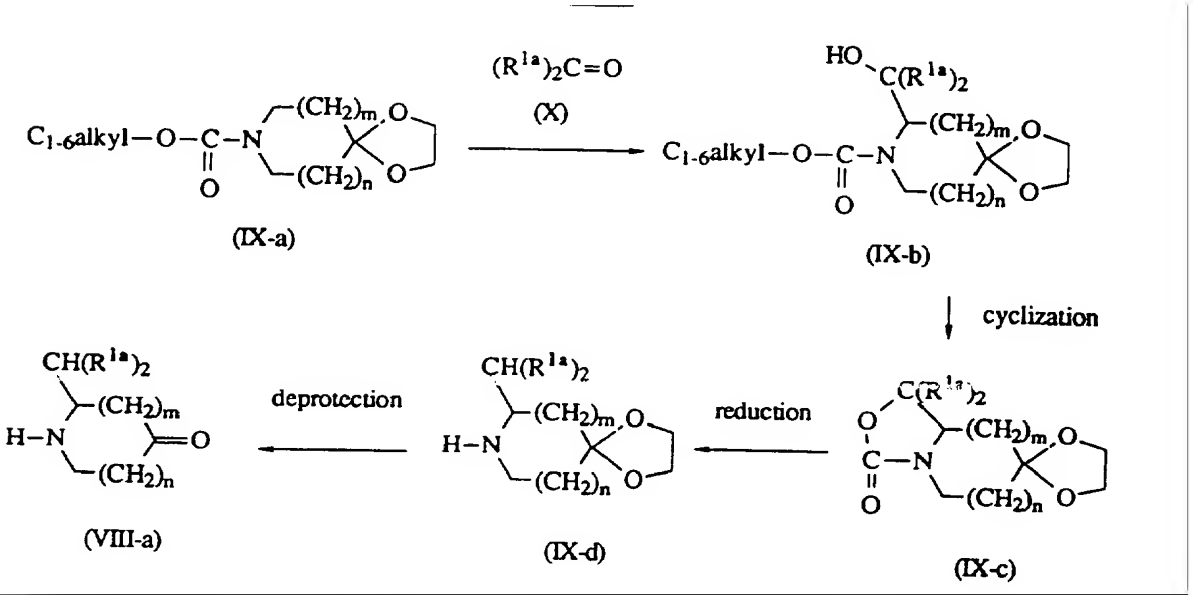
The starting materials and some of the intermediates are known compounds and are commercially available or may be prepared according to conventional reaction procedures generally known in the art. For example, intermediates of formula (III), (IV) and (VI) may be prepared according to art-known procedures.

Intermediates of formula (II) may be prepared by condensing an intermediate of formula (IV) with an intermediate of formula (VIII) analogous to the procedure described in EP-0,532,456-A.



The preparation of intermediates of formula (VIII) is also described in EP-0,532,456-A. However, intermediates of formula (VIII) wherein R^1 is optionally substituted Ar^1C_{1-6}alkyl or di(Ar^1)C_{1-6}alkyl, said R^1 being represented by -$CH(R^{1a})_2$ and said intermediates being represented by formula (VIII-a), may also be prepared as depicted in scheme 1.

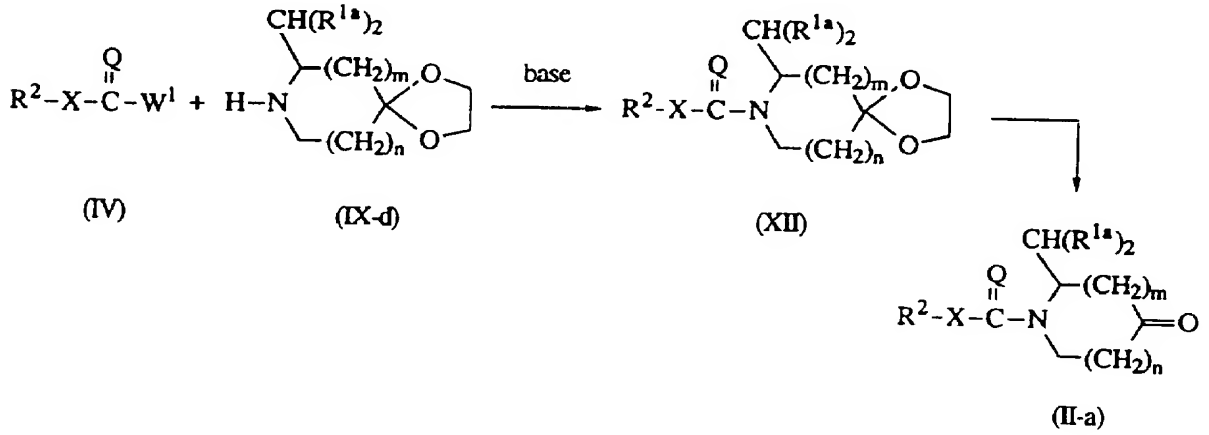
Scheme 1



In scheme 1, the intermediates of formula (IX-b) may be prepared by reacting an intermediate of formula (IX-a) with an aldehyde or a ketone of formula (X). The C_{1-6}alkylcarbamate moiety in the intermediates of formula (IX-b) may be converted into a fused oxazolone which in turn may be reduced to an intermediate of formula (IX-d). Said intermediate (IX-d) may in

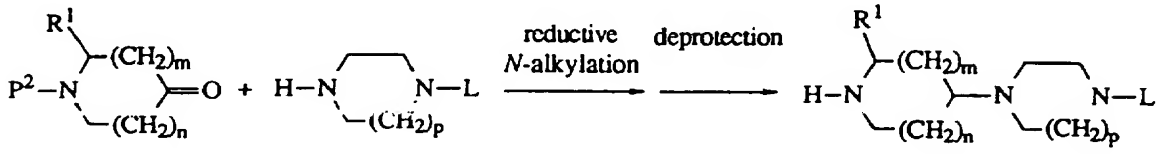
turn be deprotected, thus forming an intermediate of formula (VIII-a). Subsequently, intermediates of formula (VIII-a) may be reacted with an intermediate of formula (IV) to prepare intermediates of formula (II) wherein R^1 is defined as $-CH(R^{1a})_2$, said intermediates being represented by formula (II-a).

Said intermediates of formula (II-a) may also be prepared by first reacting intermediate (IX-d) with intermediate (IV) in the presence of a suitable base to form an intermediate of formula (XII), which may subsequently be deprotected. These reactions and those performed in scheme 1 may all be conducted following conventional methods that are generally known in the art.



(IV) (IX-d) (XII) (II-a)

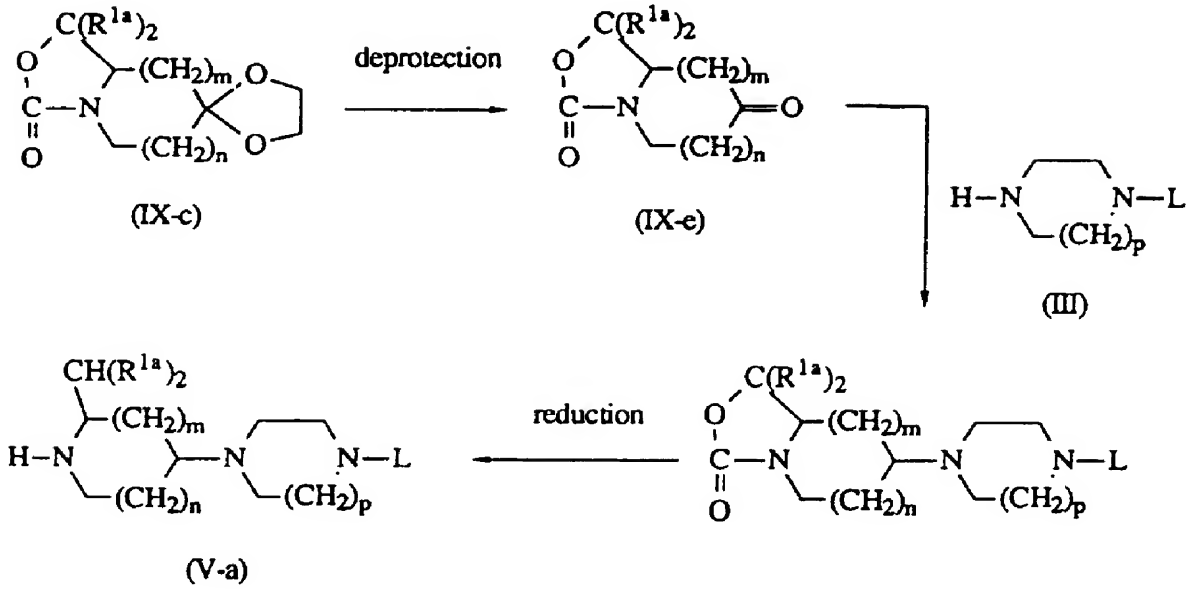
Intermediates of formula (V) may suitably be prepared by reacting an intermediate of formula (VIII-1), being a protected intermediate of formula (VIII) with a protecting group P^2 such as, for example, a C_{1-6}alkyloxycarbonyl group, with an intermediate of formula (III) according to the previously described reductive *N*-alkylation procedure, and subsequently deprotecting the thus formed intermediate.



(VIII-1) (III) (V)

In particular, intermediates of formula (V) wherein R^1 is $-CH(R^{1a})_2$, said intermediates being represented by formula (V-a), may be prepared as is depicted in scheme 2.

Scheme 2



The ketalized intermediate of formula (IX-c) may be transformed to the corresponding ketone of formula (IX-e) which subsequently may be reductively aminated with a piperazine- or homopiperazine derivative of formula (III). The thus obtained intermediate may then be reduced with a suitable reducing agent to an intermediate of formula (V-a).